Journal of the American College of Cardiology
© 2002 by the American College of Cardiology Foundation
Published by Elsevier Science Inc.

Vol. 40, No. 7, 2002
ISSN 0735-1097/02/$22.00
PII S0735-1097(02)02105-8

Influence of Wall Stress and Left Ventricular Geometry on the Accuracy of Dobutamine Stress Echocardiography

Satoshi Yuda, MD, PHD, Vincent Khoury, MB, BS, Thomas H. Marwick, MB, BS, PHD, FACC
Brisbane, Australia

OBJECTIVES The goal of this study was to determine whether wall stress at rest and during stress could explain the influence of left ventricular (LV) morphology on the accuracy of dobutamine stress echocardiography (DSE).

BACKGROUND The sensitivity of DSE appears to be reduced in patients with concentric remodeling, but the cause of this finding is unclear.

METHODS We studied 161 patients without resting wall motion abnormalities who underwent DSE and coronary angiography. Patients were classified into four groups according to relative wall thickness (normal <0.45) and LV mass (normal ≤ 131 g/m^2 in men and ≤ 100 g/m^2 in women): normal geometry, concentric remodeling, concentric hypertrophy, and eccentric hypertrophy. Significant coronary artery disease was defined as $\geq 50\%$ stenosis. Circumferential (cESS) and meridional end-systolic wall stress (mESS) were calculated at rest and peak DSE.

RESULTS Both false-negative and false-positive results for DSE were present in 35 patients (22%). The accuracy of DSE in patients with concentric remodeling (61%) was lower than that in patients with normal geometry (85%, $p < 0.05$) or concentric hypertrophy (86%, $p < 0.05$), but the accuracy with eccentric hypertrophy (64%, $p < 0.05$) was lower than with concentric hypertrophy. Patients in lowest quartile of cESS and mESS at peak had significantly lower sensitivity and accuracy than those in the highest quartile. A reduced cESS at peak ($p = 0.012$), presence of concentric remodeling ($p = 0.044$), and eccentric hypertrophy ($p = 0.012$) were significant predictors of both false-negative and false-positive results for DSE.

CONCLUSIONS The accuracy of DSE is influenced by the LV geometric pattern and peak wall stress. (J Am Coll Cardiol 2002;40:1311–9) © 2002 by the American College of Cardiology Foundation

Dobutamine stress echocardiography (DSE) has a high sensitivity (70% to 96%) and specificity (66% to 100%) (1) for the detection of coronary artery disease (CAD), even in patients with left ventricular (LV) hypertrophy (1,2). However, despite technical advances, there remain a significant number of DSE examinations with false-negative and false-positive results. Previous studies (1–3) have indicated a number of potential sources of false-negative and false-positive results. A recent study by Smart et al. (4) showed that the sensitivity of DSE is reduced in the subset of patients with LV hypertrophy who have concentric remodeling. We sought to confirm the influence of LV geometry on the accuracy of DSE and to determine the influence of wall stress on accuracy.

METHODS

Patient population. Between September 1998 and April 2000, dobutamine stress echocardiography (DSE) was performed in 1,031 patients with known or suspected CAD. Of these patients, 447 with abnormal LV function (LV ejection fraction $< 50\%$) were excluded, as were 361 patients who did not undergo coronary angiography. Of the 223 patients with DSE and coronary angiography within six months, without an intervening event, 34 with LV wall motion asynergy at rest, 13 who had poor image quality, seven with asymmetrical LV hypertrophy (septal to posterior wall thickness ratio > 1.3), five who had pacemaker rhythm, and three with severe valvular disease were excluded. The remaining 161 patients (105 men; mean age 61 $\pm$ 11 years), who were considered unlikely to have myocardial infarction, were enrolled in this study.

All patients had a complete clinical history taken at recruitment. Hypertension was defined by a systolic blood pressure (BP) ≥ 140 mm Hg, a diastolic BP ≥ 90 mm Hg, or by antihypertensive drug therapy. Hypercholesterolemia was defined as total serum cholesterol >200 mg/dl or the use of lipid-lowering therapy. Diabetes mellitus was defined as fasting blood glucose >126 mg/dl or treatment with hypoglycemic drugs and/or insulin.

DSE. Dobutamine stress echocardiography was performed using a standard protocol (1,2) in all patients after obtaining informed consent. Before the infusion was begun, a resting electrocardiogram and echocardiogram were obtained in the left lateral decubitus position using commercially available ultrasound equipment (Vingmed system FiVe, General Electric Vingmed, Milwaukee, Wisconsin). Dobutamine was administered intravenously with an infusion pump at 5 μg/kg/min, and the dosage was increased every 3 min to 10, 20, 30, and, finally, 40 μg/kg/min. If 85% of the age-predicted maximal heart rate (HR) was not achieved, 0.25

From the University of Queensland, Brisbane, Australia. Supported, in part, by the National Health and Medical Research Council, Australia.

Manuscript received February 5, 2002; revised manuscript received April 16, 2002, accepted May 29, 2002.

JACC Vol. 40, No. 7, 2002
October 2, 2002:1311–9

Abbreviations and Acronyms

BP = blood pressure
CAD = coronary artery disease
cESS = circumferential end-systolic wall stress
DSE = dobutamine stress echocardiography
HR = heart rate
LV = left ventricle/ventricular
mESS = meridional end-systolic wall stress
RWT = relative wall thickness

mg of atropine was given every minute up to a maximum of 2 mg or until the target HR was achieved. Cardiac rhythm was monitored throughout the DSE, and 12-lead electrocardiogram and BP measurements were obtained at rest and the end of each stage. Standard end points were used, including conclusion of the protocol, development of severe ischemia (either severe angina or severe impairment of LV function), severe ventricular arrhythmia, hypertension (systolic BP >240 mm Hg), symptomatic hypotension, or intolerable side effects.

The LV was divided into 16 segments as recommended by the American Society of Echocardiography (5), and each segment was scored as normal, mild hypokinetic, severe hypokinetic, akinetic, or dyskinetic. All echocardiograms were interpreted by comparison of rest and stress images in quad-screen format by an experienced observer who was unaware of the patient's treatment and outcome. Segments without any deterioration induced by DSE were characterized as normal. Ischemia was identified in the presence of a new wall motion abnormality during the DSE.

Echocardiographic analysis. The septal and posterior wall thickness at end-diastole and end-systole and LV end-diastolic and end-systolic diameters were determined from M-mode or B-mode echocardiograms. Left ventricular and midwall fractional shortening at rest and peak stress were calculated using previously reported formulae (6). Relative wall thickness (RWT) was calculated as the ratio of 2 × posterior wall thickness at end-diastole/LV end-diastolic diameter. Left ventricular mass was calculated using the formula proposed by Devereux et al. (7) and normalized for body surface area (LV mass index, g/m^2). Increased RWT was defined as ≥0.45, and increased LV mass index was defined as >131 g/m^2 for men and >100 g/m^2 for women (8). The LV geometric pattern was divided into four groups of normal geometry, concentric remodeling, concentric hypertrophy, and eccentric hypertrophy, according to RWT and LV mass index (9) (Fig. 1).

Circumferential end-systolic wall stress (cESS) at rest and peak stress was calculated as previously described (10):

$$\text{cESS} = \text{Systolic BP} \times a^2 \times (1 + b^2/c^2) \times 1/(b^2 - a^2)$$

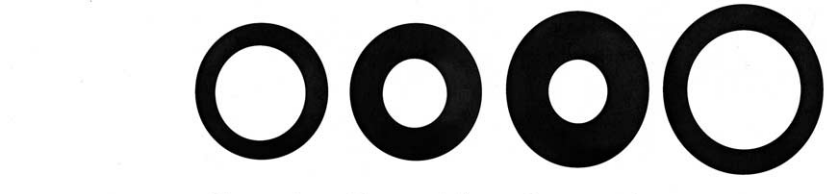
where a = (LV end-systolic dimension/2), b = (LV end-systolic dimension/2) + (posterior wall thickness at end-systole), c = (LV end-systolic dimension/2) + (posterior wall thickness at end-systole/2).

Meridional end-systolic wall stress (mESS) at rest and peak stress was calculated according to previous studies (4,11):

$$\text{mESS} = \text{Systolic BP} \times 2a \times 1/4h(1 + h/2a)$$

where h = posterior wall thickness at end-systole and a was as defined above. The end-systolic wall stress both at rest and stress were divided into quartiles for analyzing the relationship between the accuracy of DSE and the end-systolic wall stress.

Acquisition and analysis of tissue Doppler data. Gray scale images were obtained at rest, with frame rates between 80 and 120 frames/s depending on the sector width, and saved in raw data (pre-scan-converted) format. Digital storage of single cardiac cycle loops triggered to the QRS complex was saved to magneto optical disk (EDM-2300B, Sony Electronic Inc., Tochigi, Japan) and analyzed using commercial software (Echopac 6.1, General Electric Vingmed, Milwaukee, Wisconsin) by an expert reader blinded to the clinical profile and visual wall motion analysis of the patients.



	Normal Geometry (N)	Concentric Remodeling (CR)	Concentric Hypertrophy (CH)	Eccentric Hypertrophy (EH)
RWT	< 0.45	>= 0.45	>= 0.45	< 0.45
LVMI (g/m²)	=<131 (men) or =<100 (women)	=<131 (men) or =<100 (women)	>131 (men) or >100 (women)	>131 (men) or >100 (women)

Figure 1. The left ventricular (LV) geometric pattern, classified according to relative wall thickness and LV mass index. CH = concentric hypertrophy; CR = concentric remodeling; EH = eccentric hypertrophy; LVMI = left ventricular mass index; N = normal geometry; RWT = relative wall thickness.

Color tissue Doppler images from apical four-, two-chamber, and long-axis views were recorded digitally in the same way as the gray scale images.

Coronary angiography. Quantitative coronary angiography (Phillips Medical Imaging, Best, the Netherlands) was performed within six months of DSE (mean 1.7 ± 2.1 months) by an experienced angiographer who was blinded to the echocardiographic data. Significant CAD was defined as ≥50% luminal diameter stenosis in ≥1 major coronary artery.

Statistical analysis. All data are expressed as mean ± SD or frequency in percent. Differences between two groups of continuous variables were assessed by unpaired Student *t* test, and comparison among multiple groups was performed by analysis of variance with the Scheffè post-hoc test. Categorical variables were analyzed with the chi-square test, and the Fisher exact test was used when appropriate. Patients with CAD were classified into subgroups with true-positive (abnormal DSE and coronary angiography) and false-negative (normal DSE and abnormal coronary angiography) results. Sensitivity was calculated as the percent of patients with CAD showing true-positive findings on DSE. Patients without significant CAD were similarly classified into groups with true-negative or false-positive results. Specificity was calculated as the percent of patients without significant CAD who had true-negative findings on DSE. Accuracy was calculated as the portion of patients with and without angiographic evidence of CAD who were correctly identified by DSE. Sensitivity, specificity, and accuracy of DSE were also individually calculated at these different quartiles of wall stress parameters. Chi-square analysis or a Fisher exact test was used to compare the sensitivity, specificity, and accuracy in each quartile. Linear regression analysis was used to identify the correlation between LV fractional shortening and cESS and mESS at rest or peak. To determine the predictors of the lower accuracy of DSE, we divided into two groups with and without both false-negative and false-positive results for DSE. Multivariate analysis was performed to determine the independent predictors of both false-negative and false-positive results for DSE using stepwise logistic regression (SPSS version 9.0, SPSS Inc., Chicago, Illinois). Variables with a p value <0.10 (presence of concentric remodeling and eccentric hypertrophy, single-vessel left circumferential disease, cESS at peak, and mESS at peak) were entered into the multivariate model. All results were considered statistically significant when the p value was <0.05.

RESULTS

Patient characteristics. In the entire population, hypertension was documented in 73 patients, diabetes mellitus in 18, and hypercholesterolemia in 63. A number of patients were taking medical therapy; 63 were treated with beta-blockers, 29 with calcium antagonists, and 57 with nitrates.

The mean peak dose of dobutamine was 37 ± 7 μg/kg/min. Atropine was used in 82 patients (51%). The resting HR, systolic BP, and rate-pressure product were 69 ± 12 beats/min, 138 ± 24 mm Hg, and 9,698 ± 2,758 mm Hg/min, and respective values at peak stress were 132 ± 19 beats/min, 170 ± 27 mm Hg, and 22,667 ± 4,829 mm Hg/min. A total of 114 patients (71%) reached the target HR (≥85% of age-predicted maximal HR). Submaximal tests (defined by termination at less than target HR) occurred despite maximum doses in 25 patients; premature termination of the protocol occurred because of severe ischemia in 12, hypertension in three, symptomatic hypotension in two, complex ventricular premature contractions in two, nausea in two, and anxiety in one.

Coronary angiography detected significant CAD in 107 patients (66%), 61 of whom had multivessel disease. Of those with single-vessel disease, 17 had left anterior descending disease, 10 had left circumflex disease, and 19 had right CAD.

Clinical characteristics and LV geometric pattern. The clinical characteristics of patients grouped according to the LV geometric pattern are summarized in Table 1. Of the enrolled patients, 29% had normal geometry, 14% had concentric remodeling, 39% had concentric hypertrophy, and 17% had eccentric hypertrophy. There were no significant differences among LV geometric groups with regard to age, gender, body mass index, HR, BP, incidence of risk factors, and medications. The prevalence of CAD was also similar in each group.

Echocardiographic parameters and LV geometric pattern. By definition, LV mass index was increased in the groups with concentric and eccentric hypertrophy, whereas RWT was increased in the two groups with concentric LV geometric patterns (Table 2). Left ventricular and midwall fractional shortening were significantly greater in patients with normal geometry than in patients with eccentric hypertrophy. Although cESS and mESS at peak stress were similar among these groups, cESS and mESS at rest were greatest in patients with eccentric hypertrophy.

Detection of CAD from DSE. There were 63 patients with normal DSE and 98 patients with ischemia during the DSE. The sensitivity, specificity, and accuracy of wall motion abnormalities for detecting CAD were 79% (85 of 107), 76% (41 of 54), and 78% (126 of 161), respectively. Sensitivity for multivessel disease (82%, 50 of 61) was comparable with that for single-vessel disease (76%, 35 of 46, p = 0.62). In single-vessel disease, sensitivity for patients with 50% to 69% stenosis (58%, 11 of 19) was less (but not significantly so) than that with ≥70% stenosis (77%, 24 of 31, p = 0.25). Sensitivity was 95% (18 of 19) in single-vessel right CAD, 71% (12 of 17) in single-vessel left anterior descending disease, but only 50% (5 of 10, p < 0.05 vs. single-vessel right CAD) in single-vessel left circumflex disease. The positive predictive value of patients with wall motion abnormalities at single basal inferior segment was 71% (5 of 7).

Table 3 summarizes the likely causes of the 13 false-

JACC Vol. 40, No. 7, 2002
October 2, 2002:1311–9

Table 1. Clinical Characteristics of Study Patients Grouped According to Left Ventricular Geometric Pattern

	Normal Geometry (n = 47)	Concentric Remodeling (n = 23)	Concentric Hypertrophy (n = 63)	Eccentric Hypertrophy (n = 28)	p Value
Age (yrs)	59 ± 11	65 ± 13	60 ± 11	60 ± 10	0.18
Male	31 (66%)	14 (61%)	43 (68%)	17 (61%)	>0.99
Body mass index (kg/m^2)	27.1 ± 5.1	28.2 ± 4.7	28.5 ± 4.7	28.2 ± 4.8	0.50
Rest HR (beats/min)	65 ± 13	72 ± 12	71 ± 12	71 ± 15	0.08
Peak HR (beats/min)	132 ± 20	129 ± 23	133 ± 15	132 ± 24	0.78
Rest systolic BP (mm Hg)	133 ± 23	146 ± 24	137 ± 25	142 ± 21	0.20
Peak systolic BP (mm Hg)	173 ± 23	171 ± 26	170 ± 30	166 ± 30	0.83
Submaximal test	16 (34%)	5 (22%)	19 (43%)	7 (33%)	0.96
Coronary artery bypass graft	3 (6%)	2 (9%)	6 (10%)	1 (4%)	>0.99
Left bundle-branch block	2 (4%)	1 (4%)	1 (2%)	0	0.82
Single-vessel disease	16 (34%)	6 (26%)	18 (29%)	6 (21%)	0.84
Multivessel disease	18 (38%)	9 (39%)	20 (32%)	14 (50%)	0.58

Data are presented as mean value ± SD or number (%) of patients.
BP = blood pressure; HR = heat rate.

positive results for DSE; five had intermediate coronary stenosis, and two had wall motion abnormalities at single basal inferior segment. Generally, wall stress did not explain the false-positive results. In 22 patients with false-negative results for DSE, 11 had single-vessel disease, eight were treated with beta-blockers, and six had submaximal tests of DSE (Table 4). Several patients in whom the false-negative result was not otherwise explained showed low levels of wall stress.

Effects of echocardiographic parameters on accuracy of DSE. The LV mass index did not influence the accuracy of DSE for detection of CAD. The sensitivity (79% vs. 80%, p = 0.84, respectively) and specificity (79% vs. 71%, p = 0.77, respectively) were similar in groups with and without increased LV mass index. The accuracy of DSE for detection of CAD was markedly reduced by concentric remodeling (61%), compared with both normal geometry (85%, $p < 0.05$) and concentric hypertrophy (96%, $p < 0.05$). The accuracy of DSE in patients with eccentric hypertrophy was also significantly reduced in comparison with that of concentric hypertrophy (Fig. 2).

With the exception of cESS at peak (104 ± 31 kdyne/cm^2 vs. 124 ± 46 kdyne/cm^2, p = 0.02, respectively) and mESS at peak (35 ± 12 kdyne/cm^2 vs. 42 ± 17 kdyne/cm^2, p = 0.03, respectively), no statistically significant difference, including gender, beta-blockers, left bundle branch block, and single-vessel disease, was found between the group with and without both false-positive and false-negative results for DSE. Single-vessel left circumflex disease, concentric remodeling, and eccentric hypertrophy tended to be more frequent in the group with both false-positive and false-negative results.

In false-negative studies, peak cESS (103 ± 29 vs. 122 ± 38 kdyne/cm^2, p = 0.06) and peak mESS (36 ± 11 vs. 43 ± 16 kdyne/cm^2, p = 0.09) tended to be less than those with true-negative studies. No significant difference of cESS and mESS at either rest or peak stress was found between false-positive and true-positive studies for DSE.

Table 2. Echocardiographic Parameters of Study Patients Grouped According to Left Ventricular Geometric Pattern

	Normal Geometry (n = 47)	Concentric Remodeling (n = 23)	Concentric Hypertrophy (n = 63)	Eccentric Hypertrophy (n = 28)	p Value
Septal wall thickness (mm)	9.5 ± 1.1	10.8 ± 1.2*	12.8 ± 2.0*§	10.6 ± 1.3*	<0.001
Posterior wall thickness (mm)	9.2 ± 1.1	11.0 ± 1.0*	12.5 ± 1.3*†§	10.6 ± 0.9*	<0.001
Relative wall thickness	0.37 ± 0.05	0.52 ± 0.06*§	0.51 ± 0.07*§	0.39 ± 0.04	<0.001
LV mass (g)	192 ± 40	184 ± 34	297 ± 77*†	277 ± 54*†	<0.001
LV mass index (g/m^2)	100 ± 18	102 ± 17	158 ± 37*†	141 ± 19*†	<0.001
LV end-diastolic diameter (mm)	49.6 ± 3.9	42.4 ± 3.3*‡	49.3 ± 4.5	55.0 ± 3.6*†‡	<0.001
LV fractional shortening at rest (%)	37.7 ± 7.5§	36.7 ± 4.5	35.7 ± 6.6	32.1 ± 7.2	0.01
LV fractional shortening at peak (%)	37.9 ± 6.3	35.9 ± 6.6	37.5 ± 7.6	36.9 ± 5.8	0.41
Midwall fractional shortening (%)	22.7 ± 4.5§	20.5 ± 3.0	20.1 ± 4.9	18.8 ± 6.7	0.01
Circumferential ESS at rest (kdyne/cm^2)	130 ± 41	115 ± 32	114 ± 46	160 ± 46*†‡	<0.001
Circumferential ESS at peak (kdyne/cm^2)	131 ± 54	112 ± 31	111 ± 40	125 ± 40	0.11
Meridional ESS at rest (kdyne/cm^2)	48 ± 17	40 ± 12	41 ± 19	60 ± 19*†‡	<0.001
Meridional ESS at peak (kdyne/cm^2)	44 ± 19	38 ± 12	38 ± 16	44 ± 16	0.17

Data are presented as mean value ± SD or number (%) of patients. *$p < 0.05$ vs. normal geometry; †$p < 0.05$ vs. concentric remodeling; ‡$p < 0.05$ vs. concentric hypertrophy; §$p < 0.05$ vs. eccentric hypertrophy.
ESS = end-systolic stress; LV = left ventricular.

Table 3. Clinical Echocardiographic, and Hemodynamic Features of 13 Patients With False Positive Results for Dobutamine Stress Echocardiography

	Age (yrs)	Gender	WMA at Basal Inferior Segments	Intermediate Coronary Artery Stenosis	LV Geometric Pattern	Circumferential ESS (kdyne/cm^2)				Meridional ESS (kdyne/cm^2)			
						Rest	Quartile	Peak	Quartile	Rest	Quartile	Peak	Quartile
1	69	M	+		N	73	1st	113	2nd	36	2nd	43	3rd
2	41	F			N	163	4th	154	4th	65	4th	60	4th
3	71	F			CR	133	3rd	90	2nd	46	3rd	30	2nd
4	56	M			CR	73	1st	86	1st	26	1st	29	1st
5	68	F			CR	119	2nd	140	3rd	47	3rd	29	1st
6	42	M		LAD40%	CR	104	2nd	105	2nd	38	2nd	38	2nd
7	52	F			CH	108	2nd	78	1st	39	2nd	24	1st
8	66	F		LAD40%, LCX30%	CH	111	2nd	72	1st	40	2nd	22	1st
9	48	F			CH	87	1st	121	3rd	28	1st	44	3rd
10	49	F		LAD40%	CH	82	1st	71	1st	32	1st	26	1st
11	63	F	+	LAD40%, RCA30%	EH	110	2nd	94	2nd	37	2nd	30	2nd
12	44	M			EH	170	4th	64	1st	66	4th	24	1st
13	62	M		LAD40%, LCX, RCA30%	EH	128	3rd	163	4th	50	3rd	62	4th

CH = concentric hypertrophy; CR = concentric remodeling; EH = eccentric hypertrophy; F = female; LAD = left anterior descending disease; LCX = left circumflex disease; M = male; N = normal geometry; RCA = right coronary artery disease; WMA = wall motion abnormalities during dobutamine stress. Quartiles of circumferential ESS at rest = 1st: <95 kdyne/cm^2, 2nd: 95–120 kdyne/cm^2, 3rd: 121–144 kdyne/cm^2, 4th: ≥145 kdyne/cm^2. Quartiles of circumferential ESS at peak = 1st: <90 kdyne/cm^2, 2nd: 90–115 kdyne/cm^2, 3rd: 116–144 kdyne/cm^2, 4th: ≥145 kdyne/cm^2. Quartiles of meridional ESS at rest = 1st: <33 kdyne/cm^2, 2nd: 33–43 kdyne/cm^2, 3rd: 44–53 kdyne/cm^2, 4th: ≥54 kdyne/cm^2. Quartiles of meridional ESS at peak = 1st: <30 kdyne/cm^2, 2nd: 30–38 kdyne/cm^2, 3rd: 39–49 kdyne/cm^2, 4th: ≥50 kdyne/cm^2. Other abbreviations as in Table 2.

The relationship between cESS and mESS at peak stress and accuracy of DSE is summarized in Figures 3 and 4. Patients in the highest quartile of cESS had significantly higher sensitivity and accuracy than those in the lowest quartile (96% vs. 71%, $p < 0.05$ and 91% vs. 68%, $p < 0.05$, respectively) and higher sensitivity than those in the third quartile (65%, $p < 0.05$). Similarly, patients in the highest quartile of mESS at peak had significantly higher sensitivity and accuracy than those in the lowest quartile (96% vs. 71%, $p < 0.05$ and 91% vs. 65%, $p < 0.05$, respectively). Sensitivity, specificity, and accuracy of cESS and mESS at rest were comparable among each quartile.

Relationship between LV fractional shortening and parameters of wall stress. At rest, the inverse relationship of LV fractional shortening to parameters of wall stress was significant for both cESS ($r = -0.59$, $p < 0.0001$) and mESS ($r = -0.62$, $p < 0.0001$). Similarly, LV fractional shortening at peak was inversely related to both cESS ($r = -0.54$, $p < 0.0001$) at peak (Fig. 5, left) and mESS ($r = -0.57$, $p < 0.0001$) at peak (Fig. 5, right).

Predictors of both false-positive and false-negative results for DSE. Multivariate logistic regression analysis demonstrated that cESS at peak (odds ratio, 6.4; 95% confidence interval, 0.97 to 0.99, $p = 0.012$), presence of concentric remodeling (odds ratio, 4.1; 95% confidence interval, 1.01 to 9.62, $p = 0.044$), and presence of eccentric hypertrophy (odds ratio, 6.4; 95% confidence interval, 1.35 to 12.88, $p = 0.012$) were the most significant predictors of both false-positive and false-negative results for DSE.

DISCUSSION

The major findings of this study are that reduced wall stress at peak and LV geometric pattern influence the accuracy of DSE. This reduction of wall stress at peak stress may have a greater impact on the false-negative results than on the false-positive results of DSE.

LV wall stress and accuracy of DSE. Dobutamine stress echocardiography in patients with both increased wall thickness and normal LV mass index (i.e., concentric remodeling) has recently been reported to have a lower sensitivity than observed in other groups (4). The authors postulated a relationship between low sensitivity of DSE and low systolic wall stress at rest, based on the lower metabolic requirements of myocardium exposed to lower wall stress. However, the determinative measurement in this regard would be systolic wall stress at peak stress, which, in our study, was independently associated with the accuracy of DSE. Furthermore, we found a close inverse relationship between systolic wall stress and LV systolic function not only at rest, which was observed in a previous study (12), but also at peak stress. Thus, patients with low systolic wall stress at peak dobutamine have a hyperdynamic response during DSE. In this situation, the detection of a new wall motion abnormality may be difficult because of tethering effects from adjacent hyperdynamic segments. The lower

Table 4. Clinical Echocardiographic, and Hemodynamic Features of 22 Patients With False-Negative Results for Dobutamine Stress Echocardiography

	Age (yrs)	Gender	Peak Heart Rate (beats/min)	Submaximal Test	Beta-Blockers	Single-Vessel Disease	LV Geometric Pattern	Circumferential ESS (kdyne/cm^2)				Meridional ESS (kdyne/cm^2)			
								Rest	Quartile	Peak	Quartile	Rest	Quartile	Peak	Quartile
1	59	F	140		+		N	132	3rd	134	3rd	26	1st	50	3rd
2	56	M	128	+	+		N	145	4th	131	3rd	66	4th	50	3rd
3	67	M	130			LAD	N	91	1st	156	4th	35	2nd	28	1st
4	55	F	141		+	LAD	N	133	3rd	93	2nd	50	3rd	31	2nd
5	43	M	150				N	74	1st	98	2nd	26	1st	30	1st
6	69	M	131			LCX	CR	101	2nd	52	1st	39	2nd	17	1st
7	59	M	145				CR	89	1st	127	3rd	34	2nd	44	3rd
8	75	F	122			LAD	CR	79	1st	115	2nd	27	1st	47	3rd
9	37	M	159				CR	139	3rd	117	3rd	54	4th	45	3rd
10	51	F	82	+		RCA	CR								
11	48	M	146			LCX	CH	114	2nd	56	1st	42	2nd	18	1st
12	42	M	139	+			CH								
13	79	M	134			LAD	CH	124	3rd	67	1st	43	3rd	25	1st
14	74	M	129			LCX	CH	86	1st	62	1st	30	1st	20	1st
15	53	M	141				CH	82	1st	119	3rd	26	1st	43	3rd
16	68	M	141		+		EH	127	3rd	132	3rd	50	3rd	53	4th
17	60	M	97	+	+	LAD	EH	140	3rd	99	2nd	54	4th	36	2nd
18	51	F	75	+	+	LCX	EH	140	3rd	120	3rd	48	3rd	35	2nd
19	63	M	135		+		EH	159	4th	78	1st	68	4th	32	2nd
20	64	F	129			LCX	EH	250	4th	126	3rd	90	4th	46	3rd
21	62	M	60	+	+		EH	164	4th			64	4th		
22	75	F	141				EH	168	3rd	87	1st	63	3rd	33	2nd

Abbreviations as in Tables 2 and 3. The quartiles of each parameter of wall stress as in Table 3.

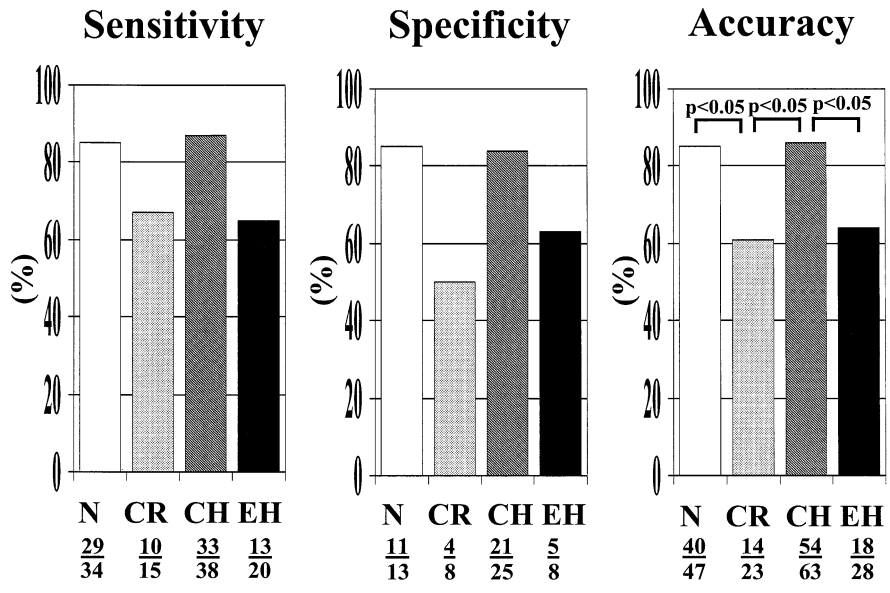


Figure 2. Sensitivity **(left),** specificity **(center),** and accuracy **(right)** of dobutamine stress echocardiography, according to the left ventricular geometric pattern. **White bars** = normal geometry (N); **light gray bars** = concentric remodeling (CR); **dark gray bars** = concentric hypertrophy (CH); **black bars** = eccentric hypertrophy (EH).

recorded sensitivity may, therefore, reflect difficulties in the recognition of inducible wall motion abnormalities due to LV cavity obliteration (13). The lower sensitivity in the setting of the lower wall stress may also be explained by the induction of less ischemia due to lower myocardial oxygen consumption. Indeed, the parallel relationship between LV wall stress and myocardial oxygen consumption has been reported in patients with hypertension and dilated cardiomyopathy (14,15). Carbon-11 acetate positron emission tomography (16) has also shown that myocardial oxygen consumption correlates closely with the rate-pressure product during dobutamine stress.

On the other hand, it may be difficult to explain how lower wall stress contributes to lower specificity of DSE (i.e., false-positive results). It is possible that angiography was performed more often in those with dilated ventricles and wall motion abnormalities. This referral bias may have increased the number of false-positive eccentric hypertrophy patients and may be a possible explanation of the lower specificity of DSE in this group. Small sample sizes used for

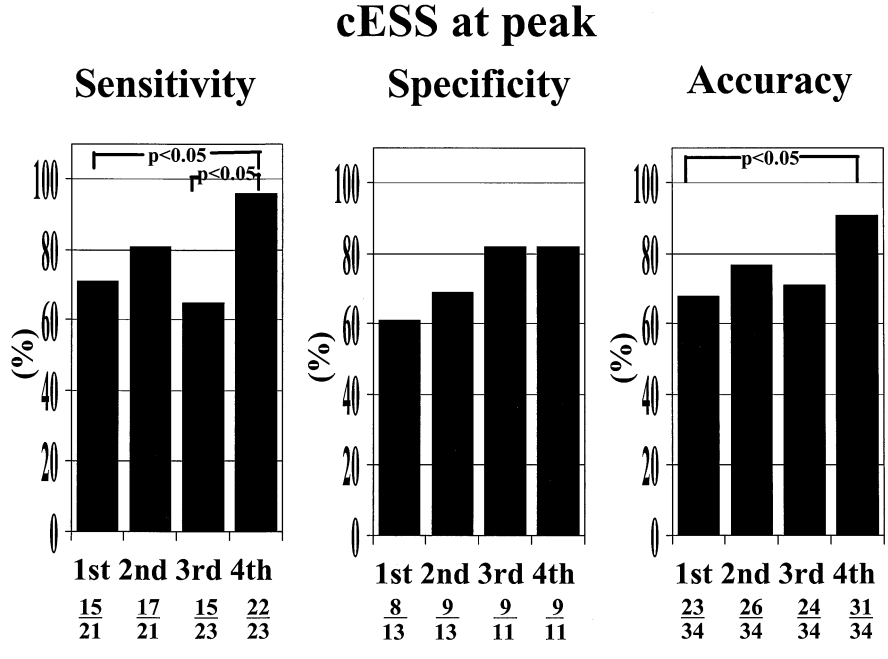


Figure 3. Sensitivity **(left)**, specificity **(center),** and accuracy **(right)** of dobutamine stress echocardiography, according to quartiles of circumferential end-systolic wall stress (cESS) at peak (1st = lowest quartile [<90 kdyne/cm^2], 2nd = 2nd lowest quartile [90 to 115 kdyne/cm^2], 3rd = 3rd lowest quartile [116 to 144 kdyne/cm^2], 4th = highest quartile [≥145 kdyne/cm^2]).

JACC Vol. 40, No. 7, 2002
October 2, 2002:1311–9

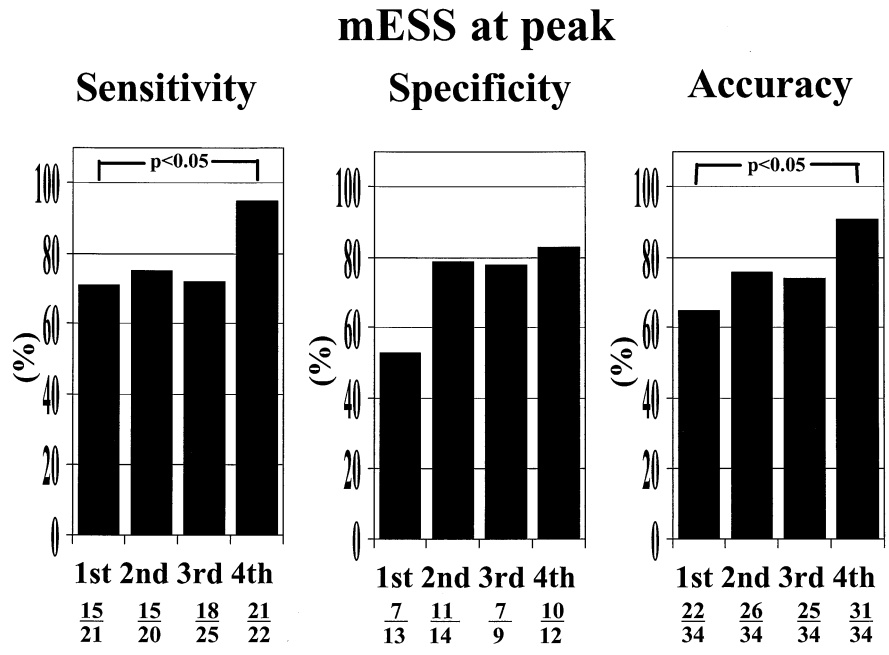


Figure 4. Sensitivity **(left),** specificity **(center),** and accuracy **(right)** of dobutamine stress echocardiography, according to quartiles of meridional end-systolic wall stress (mESS) at peak (1st = lowest quartile [<30 kdyne/cm^2], 2nd = 2nd lowest quartile [30 to 38 kdyne/cm^2], 3rd = 3rd lowest quartile [39 to 49 kdyne/cm^2], 4th = highest quartile [≥50 kdyne/cm^2]).

calculation of specificity in the concentric remodeling and eccentric hypertrophy groups may be another explanation for the apparent lower specificity in these groups. Further, wall stress at both rest and peak showed no significant difference between false-positive and true-positive studies. Thus, lower wall stress at peak dobutamine may have a lesser impact on the false-positive results for DSE.

LV geometry and accuracy of DSE. In our study, not only concentric remodeling, but also eccentric hypertrophy was associated with lower accuracy of DSE. The latter finding appears consistent with previous studies (17,18) that reported a lower specificity of dobutamine or exercise stress echocardiography in patients with dilated LV and reduced LV systolic function (e.g., dilated cardiomyopathy and severe aortic regurgitation). These conditions have a common feature of functional and structural abnormalities of the myocardium, suggesting that latent myocardial abnormalities (e.g., fibrosis) could influence the appearance of regional wall motion abnormalities with stress test. These abnormalities may be detected non-invasively with tissue velocity imaging (19).

A number of factors have been associated with false-negative and false-positive findings at DSE (1–3), but these

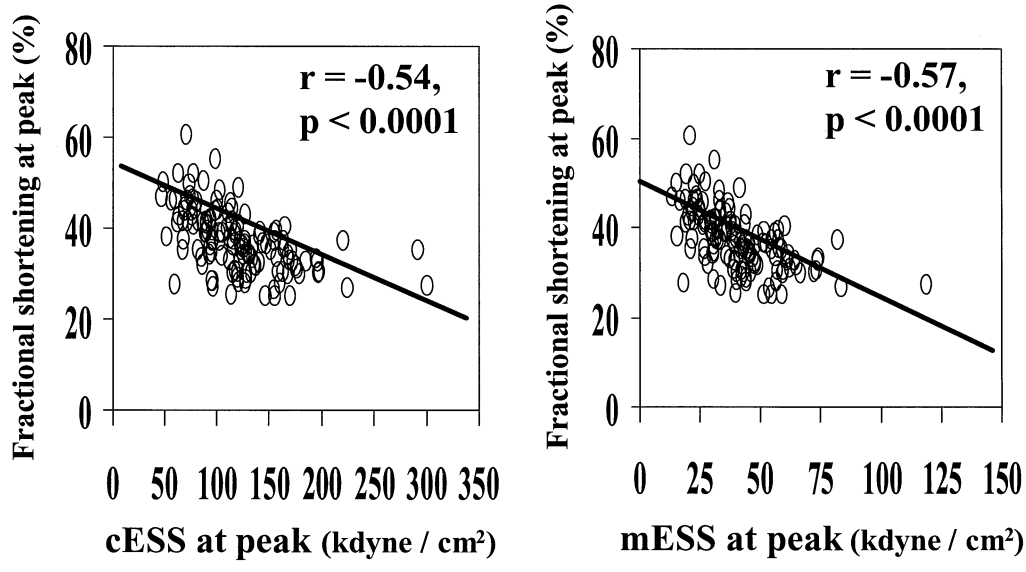


Figure 5. Correlation of left ventricular fractional shortening at peak with circumferential end-systolic wall stress at peak (cESS) **(left)** and meridional end-systolic wall stress (mESS) at peak **(right)**.

did not differ among the groups with different LV morphologies. Other possibilities, such as underestimation of coronary stenoses or coronary vasospasm during DSE (4,20), may have contributed to the findings, as LV hypertrophy is associated with reduced coronary flow reserve and increased intima-media thickness (21,22). Thus, although LV size and geometry appear to be related to the accuracy of DSE, the contribution of other factors remains unclear.

Study limitations. We could not exclude the possibility that several factors not assessed in this study, such as decreased coronary flow reserve and ischemia due to microvascular coronary disease, contributed to the results of DSE.

Clinical implications. The results of this study clarify the close relationship between the accuracy of DSE—especially with regard to sensitivity—and end-systolic wall stress at peak stress. Hyperdynamic responses that are related to this reduced end-systolic wall stress should be taken into consideration in the interpretation of DSE. From a diagnostic standpoint, wall stress at peak dobutamine and LV geometric pattern appear to influence the accuracy of DSE.

Reprint requests and correspondence: Dr. Thomas H. Marwick, University of Queensland, Department of Medicine, Princess Alexandra Hospital, Ipswich Road, Brisbane, QLD 4102, Australia. E-mail: tmarwick@medicine.pa.uq.edu.au.

REFERENCES

1. Marwick TH. Stress echocardiography. In: Topol EJ, editor. Textbook of Cardiovascular Medicine. Philadelphia, PA: Lippincott-Raven, 1998:1267–300.
2. Marwick TH, D'Hondt AM, Baudhuin T, et al. Optimal use of dobutamine stress for the detection and evaluation of coronary artery disease: combination with echocardiography or scintigraphy, or both? J Am Coll Cardiol 1993;22:159–67.
3. Bach DS, Muller DW, Gros BJ, Armstrong WF. False positive dobutamine stress echocardiograms: characterization of clinical, echocardiographic and angiographic findings. J Am Coll Cardiol 1994;24:928–33.
4. Smart SC, Knickelbine T, Malik F, Sagar KB. Dobutamine-atropine stress echocardiography for the detection of coronary artery disease in patients with left ventricular hypertrophy: importance of chamber size and systolic wall stress. Circulation 2000;101:258–63.
5. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2:358–67.
6. Shimizu G, Hirota Y, Kita Y, Kawamura K, Saito T, Gaasch WH. Left ventricular midwall mechanics in systemic arterial hypertension: myocardial function is depressed in pressure-overload hypertrophy. Circulation 1991;83:1676–84.
7. Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy finding. Am J Cardiol 1986;57:450–8.
8. Levy D, Savage DD, Garrison RJ, Anderson KM, Kannel WB, Castelli WP. Echocardiographic criteria for left ventricular hypertrophy: the Framingham Heart study. Am J Cardiol 1987;59:956–60.
9. Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. Ann Intern Med 1991;114:345–52.
10. Gaasch WH, Zile MR, Hoshino PK, Apstein CS, Blaustein AS. Stress-shortening relations and myocardial blood flow in compensated and failing canine hearts with pressure-overload hypertrophy. Circulation 1989;79:872–83.
11. Grossman W, Jones D, McLaurin LP. Wall stress and patterns of hypertrophy in the human left ventricle. J Clin Invest 1975;56:56–64.
12. Sadler DB, Aurigemma GP, Williams DW, Reda DJ, Materson BJ, Gottdiener JS. Systolic function in hypertensive men with concentric remodeling. Hypertension 1997;30:777–81.
13. Secknus MA, Niedermaier ON, Lauer MS, Marwick TH. Diagnostic and prognostic implications of left ventricular cavity obliteration response to dobutamine echocardiography. Am J Cardiol 1998;81:1318–22.
14. Cholley BP, Shroff SG, Sandelski J, et al. Differential effects of chronic oral antihypertensive therapies on systemic arterial circulation and ventricular energetics in African American patients. Circulation 1995;91:1052–62.
15. Hasenfuss G, Holubarsch C, Heiss W, et al. Myocardial energetics in patients with dilated cardiomyopathy: influence of nitroprusside and enoximone. Circulation 1989;80:51–64.
16. Porenta G, Cherry S, Czernin J, et al. Noninvasive determination of myocardial blood flow, oxygen consumption and efficiency in normal humans by carbon-11 acetate positron emission tomography imaging. Eur J Nucl Med 1999;26:1465–74.
17. Sharp SM, Sawada SG, Segar DS, et al. Dobutamine stress echocardiography: detection of coronary artery disease in patients with dilated cardiomyopathy. J Am Coll Cardiol 1994;24:934–9.
18. Wahi S, Marwick TH. Aortic regurgitation reduces the accuracy of exercise echocardiography for diagnosis of coronary artery disease. J Am Soc Echocardiogr 1999;12:967–73.
19. Shan K, Bick RJ, Poindexter BJ, et al. Relation of tissue Doppler derived myocardial velocities to myocardial structure and beta-adrenergic receptor density in humans. J Am Coll Cardiol 2000;36:891–6.
20. Varga A, Cortigiani L, Rossi PC, et al. Coronary vasospasm as a source of false positive results during dobutamine echocardiography. Cardiologia 1999;44:907–12.
21. Sekiya M, Funada J, Suzuki J, Watanabe K, Miyagawa M, Akutsu H. The influence of left ventricular geometry on coronary vasomotion in patients with essential hypertension. Am J Hypertens 2000;13:789–95.
22. Muiesan ML, Salvetti M, Zulli R, et al. Structural association between the carotid artery and the left ventricle in a general population in northern Italy: the Vobarno study. J Hypertens 1998;16:1805–12.